

### Remarks

Claims 2-5, 10-17, 31 and 33-35 are pending in the application after entry of the herein amendment. Claims 1 and 5 have been cancelled, and claims 2 and 3 amended. Support for the amendment is found in the specification at page 21, lines 10-13, and page 21, line 24 to page 23, line 23, which teaches that the starch may be heat moisture treated starch or annealing treated starch. Claims 34 and 35 are new. Support for the new claims is found in original claims 10 and 12, respectively.

Reconsideration and allowance is requested in view of the above changes, and the following remarks.

As a preliminary matter, the Office Action Summary indicates the following Disposition of Claims: claims 1-33 are pending; claims 6-9, 18-30 and 32 have been withdrawn from consideration; and claim 1-5, 10-17, 31 and 32 are subject to restriction and/or election requirement. It is respectfully submitted that the Disposition, prior to the present amendment, was incorrect. Claims 1-33 were not pending; only claims 1-5, 10-17, 31 and 33 were pending. Claims 6-9, 18-30 and 32 were not withdrawn from consideration; they were cancelled. Claims 1-5, 10-17, 31 and 32 were not subject to restriction or election, as there has been no restriction or election requirement in the application.

### Priority Document

The Office Action Summary, item 12, does not indicate that a certified copy of the British priority document has been received. Examiner is respectfully requested to check the appropriate box under item 12, which is believed to be box 3.

### Specification Objection

The specification has been amended to render browser-executable code non-executable.

### Claim Rejections - 35 USC 112

The Examiner has raised an enablement rejection with regards to the term "preventing" in

claim 2. Without acquiescing in the rejection, and solely in an effort to expedite prosecution, claim 2 has been amended to remove the word "preventing". The amendment overcomes the rejection.

#### Claim Rejections - 35 USC 102

Claims 1-3, 11-12 and 33 have been rejected as allegedly anticipated by Hansson *et al.* Claims 1-4, 13-14 and 33 have been rejected as allegedly anticipated by Schmiedel *et al.* Claims 1-3, 5, 17 and 33 have been rejected as allegedly anticipated by Bohrmann *et al.* Claims 1-3 and 31 have been rejected as allegedly anticipated by Gilbertson *et al.*

Claims 1 has been cancelled. Claims 2 and 3 have each been amended to include the feature that the starch is heat moisture-treated starch or annealing-treated starch.

#### Claims 2 and 3, 4, 10-17, 31 and 33

As taught in the present application, the inventors have found that, by using hydrothermally treated starch, *i.e.*, starches which are heat-moisture treated or annealed, the glucose release profile may be dramatically prolonged (see description page 18 lines 4-15). In the field of carbohydrate chemistry, hydrothermal treatment of starch has a very specific meaning and does not simply mean treatment in the presence of any heat and any moisture. None of the cited prior art documents describe the use of hydrothermally treated starch in methods or compositions to prevent or treat hypoglycaemia. Thus the claims prior to the present amendment, in which the starch is defined as "hydrothermally treated starch", should have been found to be novel and inventive. Nevertheless, in order to advance prosecution and remove any confusion as to the meaning of hydrothermal treatment, the claims have been amended by defining such treatment as heat-moisture treatment or annealing treatment, the two specific forms of hydrothermal treatment known in the art of carbohydrate chemistry. Indeed, the specific meaning ascribed to heat moisture treatment in the art of carbohydrate chemistry is supported by one of the documents cited by the Examiner. The Examiner has referred to Bohrmann which, in column 2, lines 14-25, clearly describes that heat-moisture-treated starch refers to specific treatments with heat under controlled moisture conditions, the conditions being such that the

starch undergoes neither gelatinization nor dextrinization.

As with heat moisture treatment, none of the cited prior art documents disclose the treatment of annealing treated starch in a treatment of hypoglycaemia, nor indeed give any hint whatsoever that such starch would have the dramatically prolonged glucose release profile which would enable it to be used in the treatment of hypoglycaemia, as demonstrated by the present inventors. Thus claims 2 and 3, and claims dependent thereon, are not anticipated by the four asserted prior art documents.

The following remarks are provided with respect to the individual references.

Hansson *et al.*

Hansson *et al.* has been cited as anticipating previous claims 1-3, 11-12 and 33. As noted above, the claims have been amended such that claim 1 has been cancelled and claims 2 and 3 have been amended to require that the starch is heat moisture treated starch (a feature of previous claim 5), or that the starch is annealing treated. As Hansson does not describe the use of heat moisture-treated starch or annealing-treated starch, the claims are clearly novel over Hansson.

Moreover, it should be noted that, although Hansson describes compositions in which starch is heat treated, the particular treatment contemplated by Hansson bears no resemblance to the claimed method utilizing heat moisture-treated starch or annealing-treated starch. Hansson's solution to the problem of treatment of hypoglycaemia in patients with diabetes or liver disease involves the use of granulated starch, in particular a starch product with minimized available surface area (see page 5 lines 23-26, claim 1 page 7 lines 19-23, etc.). The heat treated starch of Hanson is taught to be preferably in the form of baked flakes having a size of approximately 0.5-1.0 mm (see page 9 lines 22-23 and page 12 lines 8-9).

In distinct contrast, the present invention involves the use of heat moisture-treated or annealing-treated starch which enables the control of hypoglycaemia in patients, such as those with glycogen storage disease. Heat moisture-treated starch or annealing-treated starch, by virtue of their treatment, are structurally reorganized such that the release of glucose from the granules is significantly prolonged compared to normal high amylose semi-crystalline starches. Heat moisture-treated starches achieve this reorganization without the need for vastly increased

surface area to volume ratios. A heat moisture-treated (or annealing treated) starch typically has a granule of size in the range of 10-35  $\mu\text{m}$ . Thus, given that Hansson teaches that the required effect of prolonged glucose release depends on a large surface area to volume ratio, the skilled artisan would, from the teaching of Hansson, not contemplate the use of modified starch molecules having a small granule size, and thus would not contemplate using hydrothermally treated (*i.e.*, heat moisture-treated or annealing-treated) starch.

Schmiedel *et al.*

Examiner alleges the Schmiedel *et al.* anticipates claims 1-4, 13-14 and 33 as previously pending. Schmiedel is concerned with a method of preparing resistant starch, *i.e.*, starch which provides substrates for the energy metabolism of the intestinal micro flora and the large-intestine epithelial cells. Schmiedel teaches a method in which the starch is gelatinized and then reformed into a resistant starch. In contrast, as mentioned above, the method as claimed in the instant application avoids the need for gelatinization. Moreover, Schmiedel makes no mention whatsoever of the use of the starch described therein for the treatment of hypoglycaemia in any form.

Bohrmann *et al.*

The Examiner has alleged that claims 1-3, 5, 17 and 33 are anticipated by Bohrmann *et al.* Bohrmann is simply concerned with providing methods of preparing thickened food products, in particular dry food products which ultimately are added to boiling aqueous liquid and cooked therein. This document provides no teaching whatsoever of the use of such food products in the treatment of any disease, let alone hypoglycaemia associated diseases. Thus, the presently claimed invention is novel over Bohrmann.

Gilbertson *et al.*

Examiner alleges that previous claims 1-3 and 31 are anticipated by Gilbertson *et al.* As with Bohrmann, Gilbertson is simply concerned with food texture, in particular with methods of using soy products in foods with a structure substantially the same as a soy-free product made with wheat flour. There is no disclosure whatsoever of the use of that product in the treatment of any disease, let alone hypoglycaemic diseases. Gilbertson does not teach heat moisture

treatment of the starch employed therein. Indeed, the food product (dried pasta) which is "hydrothermally" treated is merely cooked in boiling water. Simply boiling starch in water does not constitute heat moisture treatment or annealing treatment.

In summary, none of the four cited prior art documents, either alone or together, provide any indication that heat-moisture treatment or annealing treatment may be employed to cause structure rearrangement in native starch granules and cause, without gelatinization. The asserted prior art does not teach that heat-moisture treated or annealing treated starch is useful as a controlled release substance for prolonging glucose release and enabling the treatment of hypoglycaemic-associated diseases, such as glycogen storage disease.

Claims 2 and 3, and dependent claims 4, 10-17, 31 and 33, are novel over the asserted prior art.

#### Claims 34 and 35

New claims 34 and 35 have been added. Claim 34 is directed to a method of treating glycogen storage disease using a waxy starch. Claim 35 is directed to a method of treating liver disease using a waxy starch.

As taught in the application as filed, the present inventors have demonstrated that waxy starches provide prolonged glucose release when ingested (see, for example, page 10, line 26 to page 11, line 25). None of the cited four prior art documents disclose advantages of prolonged glucose release associated with waxy starches, let alone their particular advantages in the treatment of glycogen storage disease or liver disease. Thus, claims 34 and 35 are both novel and inventive over the cited prior art.

With regards to claim 35 specifically, Hansson, as noted above, merely teaches the use of granulated starch in the treatment of liver disease. The granulated starch described therein is taught preferably to be corn starch (see, for example, page 7 paragraph 2). There is no mention in connection with this starch application taught by Hansson of the use of waxy starches, or indeed any indication of the prolonged glucose release profile obtainable with waxy starches, let alone the use of such waxy starches in liver disease. Accordingly, claim 35 is over Hansson et al.

Claim Rejections - 35 USC 103

The Examiner has rejected claims 1-3, 10-11, 15-16 and 33 as being unpatentable over Kaufman in view of Schmiedel. In particular, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to modify the composition of Kaufman to use hydrothermally treated waxy starch, as allegedly disclosed by Schmiedel and, by thus doing, to produce the composition as used in the methods of the previously pending claims.

As noted above, claims 2 and 3 have now been amended to include the feature that the starch is heat-moisture treated or annealing treated starch. It is noted that the Examiner has not raised an obviousness objection based on Kaufman and Schmiedel against claim 5 on which the heat moisture treatment feature of the amended claims are based.

Neither Kaufman nor Schmiedel makes any suggestion whatsoever of the potential benefits of heat-moisture treatment, or annealing treatment, with regards to the prolongation of the glucose release profile of starches, and the advantage of such starches in the treatment of diseases such as glycogen storage disease. The skilled person would therefore find no motivation to further modify the starches employed by Kaufman into heat-moisture treated (or annealing treated) starch, and thus reap the benefits obtained by the present applicants from these modifications.

Thus, the subject matter of claims 2, 3, 10-11, 15-16 and 33 would not have been obvious over Kaufman nor Schmiedel.

New claim 34 is directed to the use of waxy starches in the treatment of glycogen storage disease. As discussed above, Schmiedel merely relates to methods for producing a resistant starch but makes no mention of glycogen storage disease. Kaufman merely mentions glycogen storage disease in the introduction, specifically that corn starch has been used effectively to combat glycogen storage disease type I. No further mention is made of glycogen storage disease by Kaufman. Kaufman is specifically directed to the treatment of hypoglycaemia and type I and type II diabetes. As noted above, Kaufman makes no mention of the use of waxy starches for the treatment of diabetes, let alone the treatment of glycogen storage disease. Given that neither Kaufman nor Schmiedel provides any disclosure whatsoever of the prolongation of glucose

release profile obtained using waxy starches, let alone their potential uses in treatment of glycogen storage disease, the skilled artisan would have received no motivation to replace the corn starch (taught in the Kaufman introduction as being successfully used in the treatment of glycogen storage disease) with a waxy starch, as discussed by Schmiedel in the context of producing resistant starch which may be used as a "fat replacer" because of its decreased ability to be metabolized.

Schmiedel relates to methods of producing resistant starch, *i.e.*, starch which is resistant to metabolism (*i.e.*, that is digested less and, by definition, will release less glucose than non-resistant starch). The resistant starch is used as a "fat replacer" in certain foods. In contrast, the aim in the treatment of glycogen storage disease is to prolong glucose release to maintain glucose levels and prevent hypoglycaemia. Accordingly, the skilled artisan would not consider using the "fat replacer" compositions as taught by Schmiedel for the treatment of diseases associated with hypoglycaemia such as glycogen storage disease.

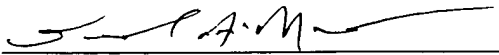
Thus, the invention of claim 34 would not have been obvious over Kaufman nor Schmiedel.

### Conclusion

The claims remaining in the application are believed to be in condition for allowance. An early action toward that end is earnestly solicited.

Respectfully submitted,

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